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Ken Inose

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EXAMINER

BERTAGNA, ANGELA MARIE

ART UNIT

PAPER NUMBER

1637

NOTIFICATION DATE

DELIVERY MODE

05/14/2008

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/553,376	Applicant(s) INOSE ET AL.	
	Examiner ANGELA BERTAGNA	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 February 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5,9 and 10 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5,9 and 10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 27, 2008 has been entered.

Claims 1-5, 9, and 10 are currently pending. In the response, claim 1 was amended, and claims 6-8 were cancelled.

Claim Rejections - 35 USC § 112, 2nd paragraph

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 9, and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite, because it is not clear from the claim language whether the salt concentration referred to in the final "wherein clause" is the salt concentration of the buffer referred to in lines 3-4, the salt concentration of the fraction obtained from gel filtration referred to in line 7, or the salt concentration of both of these solutions.

Claims 2-5, 9, and 10 are also indefinite, because they depend from claim 1.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-5, 9, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burdick et al. (EP 0 393 744 A1; cited previously) in view of Akane et al. (Biotechniques (1994) 16(2): 235, 237, 238; cited previously).

These claims are drawn to a method for isolating nucleic acids from a sample comprising eukaryotic cells, specifically a blood sample. The method comprises dissolving the sample in a buffer comprising a surfactant and a salt of a monovalent cation, heating the resulting solution at 80-100°C, and performing gel filtration to obtain a solution containing nucleic acids.

Burdick teaches methods for isolating nucleic acids from whole blood or peripheral blood mononuclear cells (see abstract and Example 2 at column 14, lines 26-44).

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Regarding claims 1, 9, and 10, the method of Burdick comprises:

(a) dissolving a sample in a buffer comprising at least one surfactant and at least one salt of a monovalent cation (column 14, lines 32-39)

(b) heating the obtained solution at 80-100°C (column 14, lines 39-41 teaches heating at 118°C; column 6, lines 33-37 teach heating at 80-120°C or 95-120°C; column 6, lines 16-19 teach heating at 100°C)

(c) filtering the heated solution (column 6, lines 52-57 and column 14, lines 41-42)

(d) collecting a solution fraction containing nucleic acids (column 6, lines 52-57 and column 14, lines 41-42).

Regarding claim 2, Burdick teaches that the surfactant is Triton X-100 (column 14, lines 37-38).

Regarding claim 3, Burdick teaches that the salt is NaCl (column 14, lines 38-39).

Regarding claims 4 and 5, Burdick teaches that the sample is a blood sample that comprises eukaryotic cells (column 14, lines 25-35).

Burdick teaches filtering the heated solution through a membrane filter (column 6, lines 52-57 and column 14, lines 41-42), but does not teach conducting a gel filtration step as required by claim 1. Also, Burdick teaches using NaCl at a concentration of 0.5 to 1.5 weight percent (86 mM – 257 mM), rather than a value within the claimed concentration range of 0.5 - 2 M.

Akane teaches methods of preparing DNA samples for PCR comprising a gel filtration step (page 235). Regarding claim 1, Akane teaches that degraded DNA and a hemoglobin derivative (hematin) isolated from forensic samples interfere with PCR amplification (page 235, column 2). Akane further teaches that although contaminating hematin may be removed by

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treatment with bovine serum albumin, ultrafiltration, chelating resin treatment, gel filtration or anion-exchange chromatography, degraded DNA may only be removed using gel filtration (page 235, column 2).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to incorporate a gel filtration step into the nucleic acid purification method taught by Burdick. Since the method of Burdick comprised a PCR amplification step following nucleic acid isolation (column 14, lines 41-44), an ordinary artisan would have been motivated to incorporate a gel filtration step, as suggested by Akane, in order to remove any contaminating degraded DNA fragments that would interfere with the PCR. An ordinary artisan would have had a reasonable expectation of success in incorporating a gel filtration step into the method of Burdick since both methods were directed to purification of DNA from forensic samples for PCR analysis.

It also would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to optimize the NaCl concentration when practicing the nucleic acid isolation method resulting from the combined teachings of Burdick and Akane. An ordinary artisan would have been motivated to optimize this results-effective variable in order to improve salt-induced precipitation of contaminating proteins present in the sample prior to the filtration step. As noted in MPEP 2144.05, "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. '[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.' *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235

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(CCPA 1955) (MPEP 2144.05).” Routine optimization is not inventive and there is no evidence to suggest that the selection of the claimed salt concentrations was other than routine or that the results should be considered unexpected compared to the closest prior art. Thus, the methods of claims 1-5, 9, and 10 are *prima facie* obvious over Burdick in view of Akane in the absence of secondary considerations.

5. Claims 1-5, 9, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. (Nucleic Acids Research (1988) 16(3): 1215; newly cited) in view of Sparkman et al. (Journal of Neurogenetics (1985) 2: 345-363; newly cited) and further in view of Goldenberger et al. (PCR Methods and Applications (1995) 4: 368-370; newly cited).

These claims are drawn to a method for isolating nucleic acids from a sample comprising eukaryotic cells, specifically a blood sample. The method comprises dissolving the sample in a buffer comprising a surfactant and a salt of a monovalent cation, heating the resulting solution at 80-100°C, and performing gel filtration to obtain a solution containing nucleic acids.

Miller teaches methods for isolating nucleic acids from a blood sample (paragraph 2).

Regarding claim 1, the method of Miller comprises:

(a) dissolving a sample in a buffer comprising at least one surfactant and at least one salt of a monovalent cation (paragraph 2)

(b) heating the obtained solution at 37°C to effect protein degradation by proteinase K (paragraph 2)

(c) precipitating proteins in the heated solution by the addition of a high concentration of salt (paragraph 2)

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(d) ethanol precipitation of nucleic acids in the solution (paragraph 2)

(e) collecting a solution fraction containing nucleic acids (paragraph 2).

Regarding claim 3, Miller teaches that the salt is NaCl (paragraph 2).

Regarding claims 4 and 5, Miller teaches that the sample is a blood sample that comprises eukaryotic cells (paragraph 2).

Miller does not teach heating the sample at 80-100°C, 90-100°C, and 95-100°C as required by claims 1, 9, and 10, respectively. Miller also teaches using a salt concentration of 400 mM rather than a concentration within the claimed range of 0.5 - 2 M. Miller also teaches the use of SDS rather than Triton X-100 as required by claim 2. Finally, Miller teaches obtaining the solution containing isolated nucleic acids by ethanol precipitation rather than gel filtration as required by claim 1.

Sparkman teaches a method of synthesizing a cDNA library from mouse neuroblastoma poly(A) RNA (see abstract and pages 347-349). Regarding claim 1, Sparkman teaches that gel filtration using a Sephadex spin column resulted in greater DNA recovery compared to ethanol precipitation (abstract and pages 359-360). Sparkman also teaches that the gel filtration step removed reverse transcriptase inhibitors that were not removed by ethanol precipitation (see pages 359-360).

Goldenberger teaches a method for isolating nucleic acids that comprises detergent lysis and proteinase K digestion (page 368, column 3 – page 369, column 1). Regarding claims 1, 9, and 10, Goldenberger teaches inactivation of proteinase K by heating at 95°C for 10 minutes (page 368, column 3). Regarding claim 2, Goldenberger teaches detergent-mediated lysis with SDS or Triton X-100 (page 368, column 3 - page 369, column 1).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to apply the teachings of Sparkman and Goldenberger to the nucleic acid isolation method taught by Miller. An ordinary artisan would have been motivated to substitute the ethanol precipitation step taught by Miller with a gel filtration step, since Sparkman taught that gel filtration resulted in reduced sample loss and removed polymerase inhibitors that could not be removed by ethanol precipitation (see abstract and pages 359-360). An ordinary artisan also would have been motivated to heat the salt and surfactant-containing proteinase K solution taught by Miller at 95°C for 10 minutes as taught by Goldenberger in order to inactivate the enzyme prior to performing the additional purification steps of the method. An ordinary artisan also would have been motivated to substitute Triton X-100 for the SDS taught by Miller, since Goldenberger taught that these detergents were art-recognized equivalents useful for achieving the same purpose, specifically cell lysis (page 368, column 3). As noted in MPEP 2144.06, substitution of art-recognized equivalents useful for the same purpose is *prima facie* obvious in the absence of secondary considerations. Finally, an ordinary artisan would have been motivated to optimize the NaCl concentration when practicing the method of Miller. An ordinary artisan would have been motivated to optimize this results-effective variable in order to improve the precipitation of protein contaminants. As noted in MPEP 2144.05, “Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. ‘[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.’ *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (MPEP 2144.05).” Routine optimization is not inventive

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and there is no evidence to suggest that the selection of the claimed salt concentrations was other than routine or that the results should be considered unexpected compared to the closest prior art. Thus, the methods of claims 1-5, 9, and 10 are *prima facie* obvious over Miller in view of Sparkman and further in view of Goldenberger in the absence of secondary considerations.

Response to Arguments

6. Applicant's arguments, see page 3, filed on February 27, 2008, regarding the rejection of claims 1, 2, 9, and 10 under 35 U.S.C. 102(b) as being anticipated by Pierre, have been fully considered and are persuasive. Pierre does not teach all of the elements of claim 1 as amended, and therefore, the rejection has been withdrawn.

Applicant's arguments filed on February 27, 2008, regarding the rejection of claims 1-5, 9, and 10 under 35 U.S.C. 103(a) as being unpatentable over Burdick in view of Akane, have been fully considered, but they were not persuasive. Applicant argues that one of ordinary skill in the art would not be motivated to use the claimed salt concentration (0.5 – 2 M) in the method of Burdick, since salt concentrations greater than 100 mM are known to inhibit the activity of Taq DNA polymerase (page 4). Applicant also argues that the claimed gel filtration step results in desalting of the nucleic acid sample, thereby rendering it suitable for PCR amplification, and that this benefit is neither taught nor suggested by the Burdick and Akane references (pages 4-5).

Applicant's first argument was not found persuasive, because Burdick teaches diluting the purified nucleic acid approximately 10-fold before conducting PCR amplification (see column 14, lines 45-58). Therefore, when practicing the method suggested by the combined teachings of Burdick and Akane, optimization of the NaCl concentration to values within the

claimed range (*e.g.* 0.5 M – 1.0 M) would not result in a final salt concentration inhibitory to Taq DNA polymerase activity, and an ordinary artisan would have optimized this results-effective variable with a reasonable expectation of success.

Regarding Applicant's second argument, it is noted that the claims as written do not require desalting the sample using a gel filtration step. Indeed, the claims as written indicate that salt concentration is 0.5 M – 2.0 M in the nucleic acid-containing fraction obtained after the gel filtration step. As a result, the features upon which Applicant relies (*i.e.* desalting via gel filtration to obtain a nucleic acid sample suitable for PCR amplification) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Also, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Since Applicant's arguments were not found persuasive, the rejection of claims 1-5, 9, and 10 under 35 U.S.C. 103(a) as being unpatentable over Burdick in view of Akane is maintained.

Conclusion

7. No claims are currently allowable.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Al-Soud et al. (Journal of Clinical Microbiology (2001) 39(2): 485-493) teaches

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purification of nucleic acids from blood cells using size exclusion chromatography (pages 486-487).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANGELA BERTAGNA whose telephone number is (571)272-8291. The examiner can normally be reached on M-F, 7:30 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Amb

/Cynthia Wilder/
Patent Examiner, Art Unit 1637